

Is less more with isotretinoin and acne?

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Clinical question

Is low-dose isotretinoin as effective and tolerable as conventional doses in the treatment of acne?

Bottom line

Studies show that acne improvement with low-dose (about 20 mg/d) isotretinoin is similar to that with conventional doses. Low-dose isotretinoin might reduce common side effects by 16% to 35%; it might also be associated with higher relapse rates, particularly with severe acne, possibly owing to lower total accumulated doses.

Evidence

- Three RCTs compared conventional with low dosing.
 - For 24 weeks, 60 patients with moderate acne used low (0.25 to 0.4 mg/kg daily) or conventional doses (0.5 to 0.7 mg/kg daily).¹ The low-dose group showed equivalent efficacy (acne grading and lesion counts); increased patient satisfaction (76% very satisfied vs 31%); and a higher (non-significant) 1-year relapse rate (18% vs 13%).
 - For 20 weeks, 150 patients with treatment-resistant nodulocystic acne used 0.1, 0.5, or 1 mg/kg daily.² There was equivalent improvement with all doses; 18-month relapse rates were 42%, 20%, and 10%, respectively.
 - Lower doses reduced common side effects (chapped lips, dry skin, and epistaxis) by 16% to 35%.^{1,2}
 - In 120 patients with mild to severe acne using high (1 mg/kg daily) or low (20 mg/d) doses on alternating days for 16 weeks,³ the low-dose group had a decrease in acne load (81% vs 95%) and fewer side effects.
- A large prospective study (638 patients with moderate acne; 20 mg/d for 24 weeks) reported "good results" in about 94% of patients, decreased incidence of side effects, and a 5% relapse rate at 4 years.⁴
- Smaller observational studies (doses about 20 mg/d) support these findings⁵⁻⁷; 2 studies report improved outcomes with a total cumulative dose of 120 mg/kg.^{5,7}

Context

- Isotretinoin is approved for the treatment of severe acne in patients aged 12 and older; the recommended dosage is 0.5 to 1 mg/kg divided into 2 doses daily for 4 to 5 months.⁸
- In many studies lower-dose groups reach lower total accumulated doses than the higher-dose treatment arms do, which might partly explain higher relapse rates.¹⁻³
- Recommended laboratory monitoring includes triglyceride, cholesterol, and liver transaminase levels, and complete blood count.^{9,10}

- Although there are reports of mood changes, suicidal thoughts, and suicide, no causal relationship has been proven.^{9,10}
- Isotretinoin is teratogenic and pregnancy must be prevented 1 month before, during, and after treatment.^{9,10}

Implementation

Isotretinoin is used in patients with severe, nodulocystic acne that is refractory to other treatments (eg, oral antibiotics). It is generally believed a cumulative isotretinoin dose ranging from 120 to 150 mg/kg is most effective in inducing acne remission.¹¹ If acne is less severe or if adverse effects are a concern, then a lower daily dose is a reasonable option. Handouts on acne¹² and websites on oral isotretinoin¹³ can help patients understand treatment options. A 2009 RxFiles article, accompanied by a patient follow-up sheet,¹⁴ might be helpful to clinicians.

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Competing interests

None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

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